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## The aetiology of glue ear—a case-control study

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### Summary

A case-control study was carried out to investigate many of the proposed causes of glue ear in childhood. One hundred and fifty cases with two matched controls were found to be remarkably similar in nearly all medical and social aspects of their past and present lives, thus providing no support for many of the currently held views on the aetiology of glue ear. Of the 5 factors which were found to increase the risk of a child undergoing surgery for glue ear, only one of these is thought to be related to the development of the condition, rather than to the chances of its detection. This factor was parental smoking (RR 1.64). The 4 other risk factors appear to influence the chance of glue ear being detected, diagnosed and referred for surgical treatment - the child's mother being employed outside the home, but only if the father is employed in non-manual work (RR 3.0); attending pre-school day-care (RR 2.00); having an older sibling who had been diagnosed as suffering from glue ear (RR 1.84); and having been born locally (in Oxfordshire) (RR 1.89). Possible explanations for these social and behavioural factors are discussed.

### Introduction

Glue ear (also known as serous or secretory otitis media) is a condition in which non-purulent fluid accumulates in the middle ear causing some conductive deafness. Children with glue ear often also suffer from recurrent attacks of acute otitis media (AOM). Although it is a widely held view that AOM may lead to glue ear [25,35],

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there is considerable evidence that glue ear predisposes to AOM [17,23]. Glue ear is currently the commonest reason for surgery during childhood [4], the peak ages in the UK being 5–8 years of age. Although the condition has been recognised since at least the middle of the nineteenth century, there is no general agreement as to its cause. There have, over the past one hundred years or more, been many aetiological theories which have been extensively reviewed elsewhere. The large number of diverse factors that have been considered means that further investigation of this subject is well suited to a case-control study design. The study described here attempts to examine many of the existing claims about aetiology, and to assess some previously unconsidered factors [6].

Amongst the existing claims are those with some scientific support (living in a damp, humid climate [38,40]; parental smoking [21]; being first born in a family [14]); some of indeterminate status (overcrowding [9,16,27,39]; low socioeconomic status [14,27,36]; day care attendance [14,36,39]; an allergic predisposition [7,12,14,18,28,39]); and some without support or as yet unevaluated (effects of heredity [10,39]; acute exanthemata [15,39]; infant feeding [3,13,21,30]; air travel [22,29,41]). New areas of interest considered are family characteristics (such as parental ages and work status; sexes of siblings); educational achievement of parents; ante-natal and delivery events; exposure to vaccines and X-rays; and contact with animals.

There are 3 other factors which have been suggested, the investigation of which is not suited to a case-control study design. These are air pollution [9,15]; as a consequence of the misuse of antibiotics for AOM [2,10,22,43,44]; and the failure to perform sufficient adenotonsillectomies in children [11,20,24,27,29,31,43]. Studies which have considered these theories have failed to provide any support for them [6].

## Method

### *Study design*

Between May 1981 and October 1982, the parents of each child aged 4–9 years who had undergone its first operation for glue ear within the previous 30 months in the ENT department, Radcliffe Infirmary, Oxford and was resident in Oxfordshire, were interviewed and asked about their child's medical, birth, family and social histories. For each case two controls were selected—the 'hospital' control from children attending a follow-up outpatient appointment in the general surgical or orthoptic departments (Table I) and the 'home' control from the same school class (the next child alphabetically, of the same sex). The controls matched the cases with respect to sex and age (hospital controls within 6 months; home controls within 12 months). The parents of cases and hospital controls were interviewed, using a structured questionnaire, by the author in the respective outpatient departments. Parents of home controls were interviewed by one or other of two research interviewers in the controls' own homes.

Surgery for glue ear was defined as myringotomy (with or without insertion of tympanostomy tubes) with or without adenoidectomy. The contents of the middle-ear

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TABLE I  
DIAGNOSES IN 150 MATCHED HOSPITAL CONTROLS

Strabismus	57	Undescended testes & hydrocoele	20
Amblyopia	7	Phimosis	17
Hypermetropia/Myopia	6	Abdominal hernias	9
Reduced visual acuity	6	G.I.T./G.U. conditions	6
Refraction errors	6	Cysts, pilonidal sinus	5
Ptoia	1	Others	10
	<u>83</u>		<u>67</u>

on operation were noted as 'dry', 'serous fluid' or 'glue'. Children with cleft-palate were excluded as this condition has been clearly shown to be associated with glue ear [33].

#### Subjects

The parents of only one potential case and 3 potential hospital controls declined to participate due to lack of time for the interview. The parents of potential home controls were approached for 146 of the cases (4 of the cases having left the District by that time). Of these, 13 (9%) declined to participate. A second potential control was successfully recruited in these instances. In two instances the potential home control's GP refused permission for inclusion in the study and another child from the same school class was obtained. Of the 146 controls finally identified and interviewed, four were withdrawn from the analysis as they had undergone surgery for glue ear.

The hospital controls were selected so that they would be comparable with cases as regards factors affecting health service usage, and the home controls for factors affecting accessibility and availability of services. Thus, if the frequency of a factor differs between cases and both sets of controls, this suggests the factor is specifically related to children undergoing surgery for glue ear. On the other hand, if the difference is only between cases and home controls (with no difference between cases and hospital controls), this suggests the factor is associated with children undergoing hospital care in general (and not specifically related to children with glue ear).

#### Statistical methods

The results are first presented as simple contingency tables that take no account of the matched design of the study. The two control groups are displayed separately because of the different selective biases operating on each. In addition, data obtained about the home controls are subject to information bias arising from the different interviewer and interview situation. Risk ratios for all variables were estimated (unmatched ratio of cross-products) and their significance tested (by computing a  $\chi^2$  value). Statistically significant variables ( $P < 0.05$ ) were further examined to take account of possible confounding (using the Mantel-Haenszel method of stratification). The original data concerning these variables were re-

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analysed taking into account the matched study design. 95% confidence limits and significance testing (McNemar Test) for matched relative risks were computed.

### Results

The respondents were mostly mothers (82%); of the remainder 5–6% were fathers, 11% were both parents, and 1% other relatives. There was no difference in this respect between cases and controls.

Of the 150 cases, 51 (34%) were aged 4 years–5 years 11 months; 69 (46%) 6 years–7 years 11 months; and 30 (20%) 8 years–9 years 11 months; 88 (59%) were male and 62 (41%) female. The age and sex distribution of this sample is similar to that for cases in the whole of Oxford Region (1975–1980). The same was true of the social class distribution (as determined by the father's occupation at the time of birth of the case).

#### Parents and siblings

The mean ages of both the fathers and the mothers of cases were similar to those

TABLE II  
FAMILY MEMBERSHIP AND STRUCTURE OF CASES AND CONTROLS

	Cases	Hospital controls	Home controls
Parents' ages—Father *	36.5 ± 0.5	36.4 ± 0.6	36.6 ± 0.5
(mean ± S.E.M.)—Mother	32.5 ± 0.4	32.7 ± 0.4	33.5 ± 0.4
	No. (%)	No. (%)	No. (%)
Parental relationship **			
Together	143 (96)	135 (90)	130 (91)
Separated	7 (4)	15 (10)	12 (9)
Number of children			
1	9 (6)	18 (12)	9 (6)
2	84 (56)	80 (53)	82 (58)
3	40 (27)	39 (26)	33 (23)
4 or more	17 (11)	13 (9)	18 (13)
Birth order of subject			
1	63 (42)	69 (46)	58 (41)
2	67 (45)	57 (38)	55 (39)
3 and subs.	20 (13)	24 (16)	29 (20)
Sex of older siblings			
Male	62 (56)	52 (47)	59 (48)
Female	49 (44)	59 (53)	63 (52)

N.B. Differences not significant ( $P < 0.05$ ) unless indicated.

\* The term 'father' is used to designate the male head of household and includes stepfather, and mother's common-law husband

\*\* The term 'together' describes all instances of the subject having always lived with the same two adults (including subjects adopted at a young age). 'Separated' includes all others (e.g.) single parent families, step-parents etc.

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TABLE III

PARENTS' PAST AND PRESENT OCCUPATIONS<sup>6</sup> AND COMBINATIONS OF PARENTAL WORKING STATUSES

NM, non-manual (Registrar General S.C.I. II, IIIN); M, manual (R.G.S.C. IIIM, IV,V).

	No. (%) of cases	No. (%) of hospital controls	No. (%) of home controls
Occupation at birth of subject			
Father -NM	60 (41)	68 (46)	65 (48)
-M	85 (59)	79 (54)	70 (52)
Parental work combinations			
Father (NM) -mother working	33 (56)*	23 (37)	42 (60)
-mother not working	26 (44)	40 (63)	28 (40)
(M) -mother working	37 (47)	37 (49)	33 (49)
-mother not working	42 (53)	39 (51)	35 (51)

N.B. Differences not significant ( $P < 0.05$ ) unless indicated.\*  $P < 0.05$  (comparison with hospital controls only)

of the parents of both sets of controls (Table II). A higher proportion of the older siblings of cases were male (though this was not statistically significant (n.s.)) and for all other measures of family structure only slight differences were observed. The length of parental full-time education and educational qualifications were remarkably similar between the 3 groups.

There was no significant difference between the proportions of fathers engaged in manual occupations (Table III). However, mothers of cases with work outside the home tended to be engaged in non-manual rather than manual work compared with the mothers of both controls. Any association with the working status of mothers was confined to the wives of non-manual men, and then only when compared with hospital controls ( $P < 0.05$ ).

*Preconception, pregnancy and perinatal events*

Fewer of the parents of cases had used contraception during the year preceding the subjects' conception, though this difference was not significant. Apart from this observation, the preconception period for the 3 groups were similar. No differences were observed for antenatal events (raised B.P., anaemia, antepartum haemorrhage, influenza, rubella). Exposure during pregnancy to both medical factors (scans, drugs, X-rays and amniocentesis) and non-medical factors (smoking, food fads) was similar. Data on the place of delivery, type of delivery, gestation, birth-weight and admission to a special care baby unit were also similar for the 3 groups. Proportions of infants breast-fed and the duration of breast feeding showed little difference.

*Childhood medical history and exposure to medical procedures*

There were no significant differences between the groups in the proportion with a history of allergic manifestations or having contracted the common infectious

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TABLE IV

CHILDHOOD HISTORY OF ALLERGY, INFECTIOUS DISEASES AND EXPOSURE TO VACCINES, X-RAYS AND DAY-CARE

	No. (%) of cases	No. (%) of hospital controls	No. (%) of home controls
Allergic conditions			
Infantile eczema	15 (10)	18 (12)	19 (13)
Hay fever	15 (10)	14 (9)	15 (11)
Asthma	7 (5)	4 (3)	3 (2)
Sensitivity to food/drugs	23 (15)	17 (11)	16 (11)
Infectious diseases			
Measles	34 (23)	39 (26)	28 (20)
Mumps	57 (39)	52 (35)	55 (39)
Chicken-pox	80 (54)	74 (50)	96 (68)
Rubella	45 (30)	51 (34)	36 (25)
Whooping cough	11 (7)	16 (11)	14 (10)
Immunizations			
All routine schedule	93 (63)	82 (55)	92 (65)
Pertussis	107 (71)	92 (61)	105 (74)
Measles	136 (91)	135 (90)	125 (88)
Additional non-schedule <sup>1</sup>	10 (7)	11 (7)	10 (7)
X-ray exposure			
Dental	11 (7)	13 (9)	N.A.
Head and neck	21 (14)	23 (15)	21 (15)
Day-care attendance <sup>2</sup>			
nil or low	20 (13)	35 (23)	26 (18)
medium/high	130 (87)*	115 (77)	116 (82)

N.B. Differences not significant ( $P < 0.05$ ) unless indicated.\*  $P < 0.05$  (only compared with hospital control).<sup>1</sup> Additional tetanus, BCG, smallpox, TAB, cholera.<sup>2</sup> Day-care = (av. No. of hours per week  $\times$  No. of months attended).

diseases of childhood (Table IV). Exposure to the routine immunizations and to X-rays was also similar in the three groups. Comparison of the amount of pre-school day-care attendance showed cases had attended more than controls ( $P < 0.05$  when compared with hospital controls).

#### ENT histories of parents and siblings

Parental history of having undergone tonsil and/or adenoid surgery showed remarkable similarity between the groups, with the proportion of mothers considerably higher than fathers (Table V). A higher proportion of the siblings of controls had a history of recurrent acute otitis media and recurrent tonsillitis ( $P < 0.05$ ). In addition, if older siblings only are considered, a higher proportion of those of cases had a history of glue ear. The older siblings of cases with glue ear were more likely to have been referred to ENT departments and treated surgically, than the older siblings of controls, though this difference did not achieve statistical significance.

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TABLE V  
ENT HISTORIES OF PARENTS AND SIBLINGS

	No. (%) of cases	No. (%) of hospital controls	No. (%) of home controls
Parental history of Ts and As <sup>1</sup>			
Father	40 (28)	40 (29)	38 (27)
Mother	62 (42)	60 (40)	50 (36)
Sibling history of ENT problems	(n = 210)	(n = 208)	(n = 211)
Recurrent A.O.M. <sup>2</sup>	42 (20) *	62 (30)	72 (34)
Recurrent tonsillitis	30 (14) *	45 (22)	41 (19)
Glue ear	26 (12)	16 (8)	17 (8)
Sibling treatment for glue ear	(n = 26)	(n = 16)	(n = 17)
Referral to ENT	22 (85)	12 (75)	12 (70)
Surgery	19 (73)	9 (56)	10 (59)
Older siblings history of ENT problems	(n = 84)	(n = 81)	(n = 84)
Recurrent A.O.M.	19 (23) *	31 (38)	33 (39)
Recurrent tonsillitis	19 (23) *	34 (42)	29 (35)
Glue ear	19 (23) **	8 (10)	14 (17)
Older siblings treatment for glue ear	(n = 19)	(n = 8)	(n = 14)
Referral to ENT	18 (95)	5 (63)	9 (64)
Surgery	16 (84)	5 (63)	8 (57)

N.B. Differences not significant ( $P < 0.05$ ) unless indicated.

\*  $P < 0.05$  (compared with hospital and home controls).

\*\*  $P < 0.05$  (compared with hospital control only).

<sup>1</sup> Tonsillectomy and adenoidectomy.

<sup>2</sup> Acute otitis media.

#### Home environment

Most aspects of housing conditions showed great similarity. These included the type and age of the accommodation, the occupying basis (owned, rented, tied), density of occupation and the basic amenities (bath/shower, washing machine, telephone, refrigerator). The exception to this was that a higher proportion of case

TABLE VI  
FAMILY MOBILITY DURING SUBJECT'S LIFETIME

	No. (%) of cases	No. (%) of hospital controls	No. (%) of home controls
Residence at time of subject's birth			
Oxfordshire	123 (82) *	107 (71)	106 (75)
Elsewhere	27 (18)	43 (29)	36 (25)

N.B. Differences not significant ( $P < 0.05$ ) unless indicated.

\*  $P < 0.05$  (only compared with hospital controls).

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families reported using an 'unsealed' heating system, that is, a system that emits the products of combustion (open fires, gas fires, paraffin stoves) ( $P < 0.05$ ).

A higher proportion of the families of cases were already living in Oxfordshire when the subject was born, than was true for the controls ( $P < 0.05$ ) (Table VI). Other measures of geographical mobility showed no difference. Other factors examined which also showed no difference included air travel by the subjects, possession of pets, and regular contact or close proximity to farm animals.

#### *Smoking habits of household members*

The present smoking status of the parents (smoker, ex-smoker, never-smoked) showed a small and insignificant difference between cases and controls. A smoking rate was calculated based on the number of years of the subjects life that the household member had smoked for, and the daily number of cigarettes smoked (or cigarette equivalent in the case of cigar and pipe smokers). This revealed that a slightly higher proportion of cases had been exposed to medium/high levels of smoking than had controls, but this difference failed to achieve statistical significance.

#### *Confounding and matched analysis*

The relative risks (RR) for all variables included in Tables II-VI were estimated by comparison with hospital controls and with home controls. For all but one variable the R.R. based on comparison with the hospital control was similar to that based on comparison with the home control (the exception was the effect of the mother working outside the home). Variables with RRs which proved to be statistically significant ( $P < 0.05$ ), plus that for parental smoking habits, are shown in Table VII. These variables were further examined for evidence of confounding. The

TABLE VII

RELATIVE RISKS OF GLUE EAR BASED ON UNMATCHED COMPARISON WITH HOSPITAL CONTROLS<sup>a</sup>, AND HOME CONTROLS<sup>b</sup>

Variable	R.R. <sup>a</sup>	R.R. <sup>b</sup>
Working mother	1.41	0.89
with N.M. father	2.16 *	0.85
Day-care attendance		
medium/high	2.00 *	1.47
Siblings with glue ear		
older siblings only	2.54 *	1.81
Smoking rate		
household	1.45	1.28
Residence		
born in Oxon	1.86 *	1.52
Unsealed heating system	1.59 *	1.59 *

N.B. Differences not significant ( $P < 0.05$ ) unless indicated.

\*  $P < 0.05$ .

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TABLE VIII

RELATIVE RISKS OF GLUE EAR BASED ON MATCHED COMPARISON WITH HOSPITAL CONTROLS <sup>a</sup>, AND HOME CONTROLS <sup>b</sup>

Variable	R.R. <sup>a</sup>	95% conf. limits	R.R. <sup>b</sup>	95% conf. limits
Working mother	1.36	—	0.94	—
with N.M. father	3.00 *	1.15-7.80	0.89	—
Day-care attendance (med/high)	2.00 *	1.13-3.53	1.50	—
Older siblings with glue ear	1.84 *	1.01-3.37	1.64 *	1.06-2.55
Smoking rate household	1.64 *	1.03-2.61	1.52 *	1.06-2.21
Residence born in Oxon	1.89 *	1.11-3.21	1.88 *	1.07-3.29

N.B. Relative risks not significant ( $P < 0.05$ ) unless indicated.\*  $P < 0.05$ ; \*  $P < 0.02$ ; (McNemar test).

only factor for which the estimate of RR was the result of confounding was unsealed heating (when parental smoking and birth in Oxfordshire were taken into account).

The other variables were re-examined by matched-pair analysis (Table VIII). This revealed similar findings to those from unmatched analysis (Table VII) for cases and both sets of controls, apart from parental smoking, for which the RR became significant on matched analysis. The data were further analysed on the basis of the contents of the middle-ear as found at operation. Of the 150 cases, 106 were found to have thick mucoid 'glue' in at least one ear, whilst the remaining 44 had either thin serous fluid or no fluid at all. Estimates of relative risk based on matched analysis of only those with 'glue' revealed similar findings to analysis of the complete series.

### Discussion

The main methodological problem encountered was the selection of controls. There was no ideal group of hospital patients from which to choose—those selected were the most appropriate available. As regards home controls, possible bias arising from different interviewers in a different setting from cases and hospital controls is considered to have had only an insignificant effect. This can be judged by the similarity of the relative risks obtained by comparison with each set of controls.

The size of this study means that risk factors present in 50% of controls would have a 90% chance of being detected if the relative risk associated with them was at least 2.0. However, the relative risk would have to be at least 3.5 if the factor was present in only 5% of controls. Negative findings must be interpreted in this context. The most striking finding was the similarity between cases and controls, or, to put it another way, how remarkably ordinary children with glue ear appeared to be in

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nearly all aspects of their past and present lives. There were, however, a few exceptions.

*(a) Climate*

Evidence for the effect of humidity and altitude is difficult to obtain in a localised study of this design. Oxfordshire has a local reputation as having a high prevalence of glue ear attributed to the effect of the Thames Valley; and indeed, cases were found to be associated with having been born in Oxfordshire (RR 1.89;  $P < 0.02$ ). While local climatic conditions could be responsible for such a finding, many other environmental factors could also be implicated.

*(b) Socio-economic conditions*

Previous studies of the influence of social class have failed to demonstrate any association with glue ear [27,34,36,39,42]. This was true of this study. There is, however, no reference in the literature to the influence of mothers working outside the home, a factor that appeared to be associated with glue ear (Table VIII), compared to hospital controls, if the father was employed in non-manual work (RR 3.0;  $P < 0.05$ ). However, this association with mother's employment status was not observed in comparison with home controls. There are 3 possible explanations for this difference—the association is due to chance; the risk estimate from the hospital control analysis may reflect a relative 'lack' of occupation outside the home for control mothers rather than an 'excess' for case mothers; or, information bias associated with the home interview may have led to 'over-recording' of maternal occupations by the mothers of home controls. It is not apparent from the data which of these explanations is correct. The only related information, on parental education, showed no associations with glue ear in the child.

A possible explanation for the association between glue ear and maternal employment status, where the father is employed in non-manual work, may be the family's attitude to the mother working. Wives of non-manual husbands are perhaps less likely to work for primarily financial reasons than the wives of manual men. Working for other reasons (e.g. career oriented; psychological benefits of getting out of the home) may be associated with attitudes to health and illness that differ from the attitudes of non-manual families in which the mother does not work. In turn these attitudes may be associated with the detection of glue ear and obtaining surgical treatment. In other words, the risk associated with mothers working may be explained in terms of health behaviour, rather than in terms of disease aetiology. Investigation of the effect of housing conditions has produced conflicting results in the past [9,15,16,39]. There was no clear evidence of housing conditions influencing the occurrence of glue ear in this study.

*(c) Family history*

It is difficult to obtain reliable information on the history of glue ear in parents due to the frequent changes of name the condition has undergone. If parents had suffered from glue ear, severely enough to necessitate surgery, then they would, on average, have been treated in the 1940s. At this time surgical treatment would have

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involved adeno-tonsillectomy. There was no difference in the history of this operation between case and control parents (Table V).

The siblings of cases were more likely to have been diagnosed as suffering from glue ear than the siblings of controls (RR 1.84;  $P < 0.05$ ). Conversely, a history of recurrent acute otitis media (AOM) was commoner in the siblings of controls. If these two middle-ear conditions are considered together, then any association between middle-ear disease in siblings and glue ear in the subject disappears (RR 0.77). Whilst not all children with a history of recurrent AOM have glue ear, the clinical distinction between the two is often not clear [17,23,25,35]. The initial diagnosis of glue ear is usually made by a General Practitioner, who, in negotiation with the parents, decides whether or not to refer the child for specialist attention. With over 200 GPs referring to the ENT department in this study, it would be expected that a wide range of indications for referral were being practiced. In this way, a child with a sibling with glue ear would be more likely to also be diagnosed as glue ear (rather than recurrent AOM) than a child without a 'glue ear' sibling (assuming all children from the same family attend the same GP with the same parents). This is supported by the finding that siblings of cases diagnosed as having glue ear are more likely to be referred to ENT care and be managed surgically than siblings of controls (Table V).

The risk associated with a sibling with glue ear therefore appears to be a product of the behaviour of parents and health care professionals, rather than any 'true' hereditary effect, though this requires further investigation. This is consistent with the only recently published study which has examined this factor [39].

*(d) Subjects medical history*

No association was found between any aspects of the subject's past medical history and the occurrence of glue ear. These aspects included infant feeding, common infectious diseases and allergic conditions. This study confirms the findings of several others that demonstrated the proportion of glue ear cases with a history of allergy was similar to the prevailing frequency in the general population [8,19,26,38].

*(e) Behaviour*

A significant association was found (RR 1.64;  $P < 0.05$ ) between glue ear and the smoking habits of all household members throughout the subject's life. This analysis assumes a constant level of exposure to smoke throughout the subject's life. Further study would be required to determine whether or not the risk of smoke is associated with any particular stage of childhood. This finding is consistent with a recent study in the USA [21] and other evidence about the hazards of passive smoking [1].

The reported risks of exposure to pre-school day-care have been conflicting [3,14,39]. This study suggests day-care attendance is a risk (RR 2.00;  $P < 0.02$ ), though the mechanism is unclear. Day-care may increase the likelihood of a child acquiring a middle-ear infection and subsequently being examined for evidence of glue ear, or the day-care staff may be on the lookout for evidence of glue ear and proceed to alert unsuspecting parents.

In conclusion, while this study has failed to substantiate the role of many

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biological factors in the aetiology of glue ear (with the exception of tobacco smoke), it has suggested that social and behavioural factors may be at least as, if not more, important in determining which children are detected, diagnosed and treated surgically for glue ear. The influence of such factors requires further investigation to support such a claim.

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